

REMARKS

Claims 29–34 and 36–42 are pending.

Amendment to the Drawings

Please replace Figure 5 with the attached figure. Figure 5 is amended to correct a typographical error. In the original figure, the nucleic acid and protein sequences were truncated at amino acid 194. The replacement figure includes amino acids 195-198 and the “stop” codon “TAA”. This amendment is made to align Figure 5 with the sequence listing.

Applicants submit that the above amendment does not represent new matter as it merely corrects an obvious typographical error. The sequence of p27 was well known to skilled artisans at the time of filing of the priority application to which the present application claims priority.

In support of this position, applicants submit the relevant pages of PCT publication WO 9602140A1, which is cited on page 7 at line 23 as describing cDNA encoding p27. This application has a publication date of February 1, 1996, which is before the priority date of the present application. Page 17 of the WO 9602140A1 publication states that Figures 15A and 15B list the cDNA sequence and encoded sequence of human kip1 (p27). Figure 15B shows the encoded sequence as consisting of 198 amino acids. Amended Figure 5 correctly shows the previously known sequences for the cDNA and encoded sequences of p27.

Sequence Listing

In response to the request for a paper and computer readable form sequence listing, applicants include a statement that the computer readable form in this application is identical with that filed in application number 08/897,333, filed June 1, 2000. Applicants request that the computer readable form filed in that application be used as the computer readable form for the instant application.

Applicants also include a paper copy of the Sequence Listing filed in application number 08/897,333. The content of this paper copy and the computer readable form are the same and contain no new matter. Applicants request that the Sequence Listing be entered into the specification.

Rejection Under 35 U.S.C. §112, second paragraph

Claims 29-34 and 36-42 are rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter regarded as the invention. Claim 1 is considered unclear as to whether the nucleic acid is administered with the balloon catheter.

The applicants respectfully traverse this rejection. However, to speed up prosecution and without prejudice or disclaimer of the subject matter claimed therein, the applicants amend claim 29 to recite that the balloon catheter is for administration of the nucleic acid. This amendment contains no

new matter and is supported, *inter alia*, by the specification at page 12, lines 16-17. Applicants submit that this amendment overcomes the 35 U.S.C. §112, second paragraph, rejection and respectfully request that the withdrawal of this rejection.

Conclusions

Applicants have overcome each of the Examiner's rejections. The application is therefore in condition for allowance and early notice to this effect is earnestly solicited. If, for any reason, the Examiner is unable to allow the application and feels that an interview would be helpful to resolve any remaining issues, he is respectfully requested to contact the undersigned attorney at (312) 321-4229.

Respectfully submitted,

Dated: OCTOBER 12, 2004


A handwritten signature in black ink, reading "John Murray", is written over a horizontal line.

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Amendments to the Drawings:

The attached sheet of drawings includes the amendments to Figure 5 and replaces the original sheet including Figure 5.

Attachment: Replacement Sheet

PCTWORLD INTELLECTUAL
Internal

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(54) Title: ISOLATED p27 PROTEIN AND METHODS FOR ITS PRODUCTION AND USE

(57) Abstract

An isolated protein designated p27 is disclosed. The p27 protein has an apparent molecular weight of about 27 kD, and is capable of binding to and inhibiting the activation of a cyclin E - Cdk2 complex. A nucleic acid sequence encoding p27 protein is disclosed, as well as a method for producing p27 in cultured cells. *in vitro* assays for discovering agents which effect the activity of p27 are also provided. Methods of diagnosing and treating hypoproliferative and hyperproliferative disorders are provided.

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Kip1.

Figures 11A and 11B

Kip1 inhibits activation of Cdk2 in vitro. Extracts from
5 exponentially growing A549 cells were incubated with
baculovirally expressed histidine-tagged cyclin E alone
or together with Kip1. Cyclin E complexes were then
retrieved with Ni²⁺-NTA-agarose, and assayed for histone
H1 kinase activity (A), and by western immunoblotting
10 using anti-Cdk2 antibody (B). Kinase activity was
quantitated by Phosphorimager and expressed as arbitrary
units. In B, Cdk2* indicates the faster migrating form of
Cdk2 that corresponds to Cdk2 phosphorylated at Thr¹⁶⁰ (Gu
et al., 1992).

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Figures 12A and 12B

Expression pattern of Kip1 in various tissues and cell
proliferation states. Kip1 Northern blots using equal
amounts of poly(A)⁺ RNA from the indicated human tissues
20 (A) or from Mv1Lu cells in different proliferation states
(B). The latter blot was rehybridized with a
glyceraldehyde-phosphate dehydrogenase probe.

Figures 13A and 13B

25 Mink Kip1 cDNA and the encoded mink kip1

Figures 14A and 14B

Mouse Kip1 cDNA and the encoded mouse kip1

30 Figures 15A and 15B

Human Kip1 cDNA and the encoded human kip1

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FIGURE 15A

ATG TCA AAC GTG CGA GTG TCT AAC GGG AGC CCT AGC CTG GAG CGG ATG Met Ser Asn Val Arg Val Ser Asn Gly Ser Pro Ser Leu Glu Arg Met 1 5 10 15 48
GAC GCC AGG CAG GCG GAG CAC CCC AAG CCC TCG GCC TGC AGG AAC CTC Asp Ala Arg Gln Ala Glu His Pro Lys Pro Ser Ala Cys Arg Asn Leu 20 25 30 96
TTC GGC CCG GTG GAC CAC GAA GAG TTA ACC CGG GAC TTG GAG AAG CAC Phe Gly Pro Val Asp His Glu Glu Leu Thr Arg Asp Leu Glu Lys His 35 40 45 144
TGC AGA GAC ATG GAA GAG GCG AGC CAG CGC ANG TGG AAT TTC GAT TTT Cys Arg Asp Met Glu Glu Ala Ser Gln Arg Lys Trp Asn Phe Asp Phe 50 55 60 192
CAG AAT CAC AAA CCC CTA GAG GGC ANG TAC GAG TGG CAA GAG GTG GAG Gln Asn His Lys Lys Pro Leu Glu Gly Lys Tyr Glu Trp Gln Glu Val Glu 65 70 75 80 240
AAG GGC AGC TTG CCC GAG TTC TAC TAC TAC TAC TAC TAC TAC TAC TAC Lys Gly Ser Ser Leu Pro Glu Phe Tyr Tyr Tyr Tyr Tyr Tyr Tyr Tyr 85 90 95 288
GGT GCC TGC AAG GTG CCG GCG CAG GAG AGC CAG GAT GTC AGC GGG AGC Gly Ala Cys Lys Lys Val Pro Ala Gln Glu Ser Gln Asp Val Ser Gly Ser 100 105 110 336

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FIGURE 15B

CGC CCG GCG GCG CCT TTA ATT GGG GCT CCG GCT AAC TCT GAG GAC ACG Arg Pro Ala Ala Pro Leu Ile Gly Ala Pro Ala Asn Ser Glu Asp Thr 115 120 125	384
CAT TTG GTG GAC CCA AAG ACT GAT CCG TCG GAC AGC CAG ACC GGG TTA His Leu Val Asp Pro Lys Thr Asp Pro Ser Asp Ser Gln Thr Gly Leu 130 135 140	432
GCG GAG CAA TGC GCA GGA ATA AGG AAG CGA CCT GCA ACC GAC GAT TCT Ala Glu Gln Cys Ala Gly Ile Arg Lys Arg Pro Ala Thr Asp Asp Ser 145 150 155	480
TCT ACT CAA AAC AAA AGA GCC AAC AGA ACA GAA GAA AAT GTT TCA GAC Ser Thr Gln Asn Lys Arg Ala Asn Arg Thr Glu Glu Asn Val Ser Asp 160 165 170 175	528
GGT TCC CCA AAT GCC GGT TCT GTG GAG CAG ACG CCC AAG AAG CCT GGC Gly Ser Pro Asn Ala Gly Ser Val Glu Gln Thr Pro Lys Lys Pro Gly 180 185 190	576
CTC AGA AGA CGT CAA ACG TA Leu Arg Arg Arg Gln Thr 195	597

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